

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A method for evaluating the morphogenic activity of a candidate morphogenic protein or analog thereof, comprising:
 - (a) creating in a mammal a local defect site ~~in a mammal~~ accessible to progenitor cells,
 - (b) administering at least 6 hours after creating the local defect site, said candidate morphogenic protein or analog thereof systemically to said mammal at a site distal from the local defect site,
 - (c) measuring the ability of said candidate morphogenic protein or analog thereof to induce new tissue formation at said defect site, and
 - (d) comparing the ability of said candidate morphogenic protein or analog thereof with the ability of a control to perform the same function,wherein said local defect site is in renal, skeletal, lung, cardiac, liver, pancreas, uterine, ovarian, gastrointestinal, colon, dermal, osteochondral, chondral, or thyroid tissue, and wherein the evaluation of said candidate morphogenic protein or analog thereof is based on the difference between the ability of said candidate morphogenic protein or analog thereof, and the ability of a control compound to induce new tissue formation at said defect site.
2. **(Canceled)**
3. **(Currently amended)** A method for evaluating an optimal dosage of a candidate morphogenic protein or analog thereof for administering to a mammal, comprising:
 - (a) creating in a mammal a local defect site ~~in a mammal~~ accessible to progenitor cells,
 - (b) administering at least 6 hours after creating the local defect site, said candidate morphogenic protein or analog thereof at a dosage to be tested systemically to said mammal at a site distal from the local defect site,
 - (c) measuring the ability of said candidate morphogenic protein or analog thereof to induce new tissue formation at said defect site, and

(d) comparing the ability of said candidate morphogenic protein or analog thereof with the ability of a control to perform the same function, wherein said local defect site is in renal, skeletal, lung, cardiac, liver, pancreas, uterine, ovarian, gastrointestinal, colon, dermal, osteochondral, chondral, or thyroid tissue, and wherein the evaluation of said candidate morphogenic protein or analog thereof is based on the difference between the ability of said candidate morphogenic protein or analog thereof, and the ability of a control compound to induce new tissue formation at said defect site.

4. **(Canceled)**
5. **(Withdrawn)** The method of claim 1 or 3, wherein said non-neuronal defect site occurs in skeletal, lung, cardiac, liver, pancreas, uterine, ovarian, gastrointestinal, colon, dermal, oral mucosa, osteochondral, chondral, or thyroid tissue.
6. **(Previously presented)** The method of claim 1 or 3, wherein said defect site occurs in renal tissue.
7. **(Withdrawn)** The method of claim 1 or 3, wherein said defect site occurs in dental or periodontal tissue.
8. **(Previously presented)** The method of claim 1 or 3, wherein said mammal is aged.
9. **(Previously presented)** The method of claim 1 or 3, wherein said mammal has a reduced capacity to induce callus formation.
10. **(Previously presented)** The method of claim 1 or 3, wherein said mammal is afflicted with impaired blood flow to the skeletal extremities.
11. **(Previously presented)** The method of claim 1 or 3, wherein said mammal has a reduced capacity to induce an endogenous morphogenic signal.
12. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein or analog thereof is administered parenterally.

13. **(Previously presented)** The method of claim 12, wherein said morphogenic protein or analog thereof is administered intravenously.
14. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein or analog thereof is administered orally.
15. **(Previously presented)** The method of claim 1, wherein said morphogenic protein or analog thereof is administered to said mammal at a time when mesenchymal progenitor cells are accessible to said local defect site.
16. **(Canceled)**
17. **(Previously presented)** The method of claim 1, wherein said morphogenic protein or analog thereof is administered at least 24 hours after the creation of said local defect site.
18. **(Previously presented)** The method of claim 1, wherein said morphogenic protein or analog thereof is administered at least 72 hours after the creation of said local defect site.
19. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein or analog thereof is administered to said mammal after the initiation of fibrosis at said local defect site.
20. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein or analog thereof is administered in aqueous solution.
21. **(Previously presented)** The method of claim 8, wherein said mammal is a steroidal drug user.
22. **(Previously presented)** The method of claim 8, wherein said mammal is aged, obese, hypertensive, or afflicted with osteopenia or diabetes.
23. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen selected from: OP1, OP2, OP3, BMP2, BMP3, BMP4, BMP5, BMP6, BMP9, BMP-10, BMP-11, BMP-12, BMP-15, BMP-3b, DPP, Vg1, Vgr-1, 60A protein, GDF-1, GDF-3, GDF-5, GDF-6, GDF-7, GDF-8, GDF-9, GDF-10, or GDF-11.

24. **(Previously presented)** The method of claim 23, wherein said morphogen is selected from: OP1, OP2, BMP2, BMP4, BMP5, or BMP6.
25. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein is a morphogenically active amino acid sequence variant of a morphogen comprising an amino acid sequence having at least 70% homology within the C-terminal 106 amino acids, including the conserved seven cysteine domain, of human OP1.
26. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein is OP1.
27. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein is mature OP1 solubilized in a saline solution.
28. **(Previously presented)** The method of claim 1 or 3, wherein said morphogenic protein comprises an amino acid sequence defined by OPX (SEQ ID No. 3); Generic Sequence 6 (SEQ ID No. 4), Generic Sequence 7 (SEQ ID No. 5); Generic Sequence 8 (SEQ ID No. 6); or Generic Sequence 9 (SEQ ID No. 7).
29. **(Withdrawn)** A method for inducing new tissue formation at a nonskeletal defect locus in a mammal, comprising administering morphogenic protein systemically to said mammal.
- 30-75. **(Canceled)**
76. **(Withdrawn)** A method for inducing bone or cartilage formation at a defect locus in a mammal, comprising administering osteogenic protein systemically to said mammal.
- 77-122. **(Canceled)**
123. **(Previously presented)** The method of claim 3, wherein the local defect site is a permissive defect site.
124. **(Previously presented)** The method of claim 1, wherein the ability of said candidate morphogenic protein or analog thereof to induce new tissue formation is measured by

observation of actual new tissue formation by histological examination of the local defect site.

125. **(Currently amended)** A method for evaluating tissue regeneration activity of a candidate morphogenic protein or analog thereof, comprising:

- (a) creating in a mammal a local defect site ~~in a mammal~~ accessible to progenitor cells,
- (b) administering, at least 6 hours after creating the local defect site, said candidate morphogenic protein or analog thereof systemically to said mammal at a site distal from the local defect site,
- (c) measuring the extent of replacement tissue regeneration at the local defect site induced by the administration of said candidate morphogenic protein or analog thereof, and
- (d) comparing the extent of replacement tissue regeneration at the local defect site induced by the administration of said candidate morphogenic protein or analog thereof with the extent of tissue regeneration induced by the administration of a control,

wherein said local defect site is in renal, skeletal, lung, cardiac, liver, pancreas, uterine, ovarian, gastrointestinal, colon, dermal, osteochondral, chondral, or thyroid tissue, and wherein the evaluation of said candidate morphogenic protein or analog thereof is based on the difference between the ability of said candidate morphogenic protein or analog thereof, and the ability of a control compound to induce new tissue formation at said defect site.